IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gerald Horn
Appl. No.: 09/854,414
Conf. No.: 7675
Filed: May 10, 2001
Title: OPHTHALMIC FORMULATIONS
Art Unit: 1618
Examiner: Z. Ray
Docket No.: 114309-1007

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AFFIDAVIT OF GERALD HORN, M.D.

I, Gerald Horn, hereby states as follows:

1. I am the sole inventor of the above-referenced U.S. Patent Application No. 09/854,414.

2. I have reviewed the Final Office Action issued on September 11, 2007 regarding this case, a copy of which is attached herewith as Exhibit A. In particular, I have reviewed U.S. Patent No. 4,443,441 (Galin) as referenced in the Final Office Action on page 2, a copy of which is attached herewith as Exhibit B.

3. Of the presently pending claims, claim 74 is the sole independent claim. Claim 74 is directed to an ophthalmic, night vision formulation. The formulation includes a sterile aqueous carrier; and a pharmaceutically active compound consisting essentially of phentolamine in a therapeutically effective amount so as to effectively disrupt endogenous compounds which stimulate dilator muscles of a human eye thereby effectively reducing pupil size to improve night vision.

4. The claimed phentolamine-based formulation inhibits pupillary dilation in scotopic conditions preferentially over constriction of the pupil, affecting the dilator muscles of the iris preferentially, and has no clinically significant effect on the ciliary muscle responsible for accommodation. Therefore, pupil size is optimized to obtain enhanced vision acuity in dim light (e.g., at night) by reducing the pupil diameter in dim light. Moreover, this result was unexpected

since conventional ophthalmology indicated that reducing pupil size in dim light would cau vision acuity to deteriorate.

5. I also conducted experiments that demonstrated the beneficial effects of t phentolamine-based formulation as claimed. For example, Table 1 on page 27 of the prese application indicates that the phentolamine-based formulation demonstrates enhanced pu reduction effect while minimizing eye redness as compared to other types of alpha-1 antagon based formulations. Further, Table 2 on page 28 of the present application demonstrates t beneficial effects on night vision by reducing the pupil diameter in dim light. In Table 2, t glare and halo effects were reduced in addition to an improvement in depth perception reducing the pupil diameter in dim light.

6. In contrast, Galin is directed to the use of alpha adrenergic blocking agents to a in the fixation of intraocular lenses. See, Galin, col. 1, lines 4-5. Indeed, Galin further disclos that this type of pupillary activity can reduce eccentric synechia formation and lens dislocatio See, Galin, column 1, line 61-67. Nowhere does Galin suggest that the reduction of pupil size dim light can enhance night vision in contrast to the claimed phentolamine-based formulatio Again, the reduction of pupil size to enhance night vision was contrary to convention ophthalmology as previously discussed. Moreover, nowhere does Galin suggest that phentolamine-based formulation has enhanced effects on pupil reduction in dim light, th enhancing night vision, as compared to other types of formulations. Indeed, the only workin example in Galin relates to a thymoxamine-based formulation to aid in the fixation of a intraocular lens.

I hereby declare that all statements made herein of my own knowledge are true and th all statements made on information and belief are believed to be true, and further that thes statements were made with the knowledge that willful false statements may jeopardize th validity of the application or any patent issued thereon.

Date: March 28, 2007

GERALD HORN, M.D.

Exhibit A

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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P.O. Box 1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,414	05/10/2001	Gerald Horn	HORN006CIP	7675

24573 7590 09/11/2007

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CHICAGO, IL 60690

EXAMINER	
FAY, ZOHREH A	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/854,414	HORN, GERALD	
	Examiner	Art Unit	
	Zohreh A. Fay	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11,13-15,18-28,37-40 and 43-73* is/are pending in the application.

4a) Of the above claim(s) *10,11,13-15,18-28,37-40 and 43-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 66-73 are presented for examination.

The remarks filed on June 14, 2007 have been received and entered.

Claims 66-73 are rejected under 35 U.S.C. 102 (b) as being anticipated by Galin (U.S. Patent 4,443,441) for the reasons set forth on page 2 of the office action of December 15, 2006.

Applicant's arguments and remarks have been carefully considered, but are not deemed to be persuasive. Applicant in his remarks argues the function of the claimed invention. The arguments are not well taken, considering that the claims of the instant application are composition claims. If applicant is using the same composition as prior art record, it is expected for the composition of the prior art to have the same function as the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 66-73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims19-26 of copending Application No. 10/799,299. Although the conflicting claims are not identical, they are not patentably distinct from each other because they overlap. The claims of the instant application are drawn to an alpha 1-antagonist in a pharmaceutical formulation. The claims of the copending application are drawn to specific alp 1-antagonists in a pharmaceutical formulation. The claims of the co-pending application are within the scope of the claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The newly submitted references by the applicant necessitate the new ground of rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zohreh A. Fay whose telephone number is (571) 272-0573. The examiner can normally be reached on Monday to Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Z.F

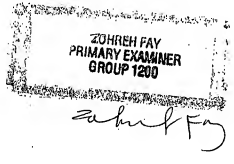

Exhibit B

United States Patent [19]

Galin

[11] **4,443,441**

[45] **Apr. 17, 1984**

[54] **FIXATION OF INTRAOCULAR LENSES**

[76] Inventor: **Miles A. Galin,** 113 E. 39th St., New York, N.Y. 10016

[21] Appl. No.: **290,854**

[22] Filed: **Aug. 7, 1981**

[51] **Int. Cl.**[3] **A61K 31/33;** A61K 31/415; A61K 31/22; A61K 31/135

[52] **U.S. Cl.** ..... **424/244;** 424/273 R; 424/273 B; 424/311; 424/330

[58] **Field of Search** ..... 424/311, 273 R, 273 B, 424/244, 330

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,658,963 4/1972 Turner et al. 424/311

OTHER PUBLICATIONS

Wand et al.-Survey of Ophth. 25(2): 75-84 (1980), "Thymoxamine Hydrochloride: An Alpha-Adrenergic Blocker".

Chem. Abst. 77, 654f (1972)—Fawke.

Chem. Abst. 78, 24240(q), (1973)—Hugues et al.

Chem. Abst. 85, 56925(e), (1976)—Wand et al.

Chem. Abst. 87, 177909(a), (1977)—Mayer et al.

Primary Examiner—Douglas W. Robinson

Attorney, Agent, or Firm—Brumbaugh, Graves, Donohue & Raymond

[57] **ABSTRACT**

The fixation of an intraocular lens is aided by instilling into an eye having an intraocular lens about one drop of an ophthalmic solution containing an α-adrenergic blocking agent, such as thymoxamine, in a concentration of from about 0.1% to about 1% by weight, preferably about 0.5% by weight.

5 Claims, No Drawings

FIXATION OF INTRAOCULAR LENSES

The present invention relates to the fixation of intraocular lenses.

An intraocular lens, when surgically implanted, is designed to replace a previously or simultaneously removed cataractous lens. There are various types of intraocular lenses, such as iris-supported lenses, anterior chamber lenses and posterior chamber lenses. The optical portion of such lenses may be of chemically pure polymethylmethacrylate or glass or any combination thereof. In an iris-supported lens the optical portion may have supports of the same nature, or may be supported by loops made of nylon, polypropylene or metal. Intraocular lenses, depending on the type, may be held in place by engagement of the loops with the iris, by angle fixation, by fixation in the lens capsular bag or by adhesions.

However, a pharmacological need exists for aiding the fixation of intraocular lenses, i.e., the maintaining or stabilizing in the correct position of intraocular lenses, the repositioning of partially dislocated intraocular lenses, and the ability to rapidly alter pupillary diameter in this regard. When pilocarpine was used as a potential fixation aid, it was found that pilocarpine causes spasms of the ciliary body termed "cyclotonia", intense constriction of the pupil through cholinergic stimulation of the sphincter muslce area, and poor and delayed reversibility. This firm contraction—squeezing on an intraocular lens—induces notching of the iris and atrophy of the sphincter area with iris-supported lens. In addition, the tight drum-like contraction precludes good fluid flow from the posterior and anterior chambers leading to debris depositing on the intraocular lens, and the potential for pupillary block, particularly with extracapsular cataract extraction. Further, the smaller pupil reduces vision, particularly in dim light.

Accordingly, it is the object of the present invention to aid the fixation of all types of intraocular lenses by compatible means.

It was found that this objective could be achieved by instilling into an eye having an intraocular lens about one drop of an ophthalmic solution containing an α-adrenergic blocking agent in a concentration of from about 0.1% to about 1% by weight. It is preferred that the ophthalmic solution contain the α-adrenergic blocking agent in a concentration of about 0.5% by weight. The approximately one drop dose can be repeated several times per day or daily, as may be necessary. Such instillation is easily reversible, permits pupillary response to light and dark and maintains passive miosis.

Suitable α-adrenergic blocking agents include tymoxamine (thymoxamine hydrochloride), phentolamine (phentolamine hydrochloride), azapetine (azapetine phosphate), phenoxybenzamine (phenoxybenzamine hydrochloride), clonidine (clonidine hydrochloride) and tolazoline (tolazoline hydrochloride). The preferred topical α-adrenergic blocking agent is tymoxamine and the preferred solvent is water.

The α-adrenergic blocking agent, such as thymoxamine, used to aid in the fixation of intraocular lenses act as a miotic and causes miosis or contraction of the pupil induced by paralysis or relaxation of the dilator muscle of the iris without contraction of the sphincter muscle of the iris. This unique pupillary activity reduces eccentric synechia formation and lens dislocation. It was further found that the α-adrenergic blocking agents are compatible with the materials from which the various types of intraocular lenses are made.

An aqueous ophthalmic solution containing about 0.5% by weight thymoxamine (available from William R. Warner & Co., Ltd., or Warner-Lambert Company) can have the following composition:

Thymoxamine Hydrochloride: 500 mg.
Sodium Acetate NF: 90 mg.
Boric Acid NF: 1610 mg.
Phenylmercuric Nitrate NF: 2 mg.
Purified Water USP q.s. to: 100 ml.

This aqueous ophthalmic solution can be prepared by dissolving the sodium acetate, boric acid and phenylmercuric nitrate in most of the purified water. Dissolution can be promoted by heating the solution. Upon cooling the solution to room temperature, the thymoxamine hydrochloride may be added and can be dissolved without further heating. The remainder of the purified water may then be added to reach a final volume of 100 ml. Sterilization of the solution can be achieved by filtering it through a sterilizing filter. This exemplary aqueous opthalmic solution has a pH of about 5.6–6 and is clear and colorless.

The process of the present invention has been satisfactorily used for aiding the fixation of all types of intraocular lenses in animals and humans.

Several advantages of using thymoxamine (or other α-adrenergic blocking agents) in the process of the present invention are noted below.

At the time of insertion of an intraocular lens in the operating room, it is desirable to dilate the pupil for posterior chamber lenses and for iris fixation lenses. Dilatation can be achieved with sympathomimetic agents and cholinergic inhibitors. The usual use of sympathomimetic agents is contraindicated, because after the procedure is finished, the pupil may dilate widely and, as a consequence, the lens may dislocate. The use of thymoxamine in the operating room to reverse the dilating effects of sympathomimetic agents is advantageous. Further, the use of thymoxamine in the placement of anterior chamber lenses where the pupil needs to be small during the insertion of the lens and wide after the insertion of the lens is advantageous, because of the ease of reversibility of the agent.

As mentioned above, the use of thymoxamine is not limited to iris-supported lenses. Posterior chamber lenses, for example, often need the pupil to be small for several days while the lens fixates itself, and the pupil may be dilated. Iris-supported lenses are probably best fixated by passive miosis so tht the pupil will move and notching will not occur.

The present invention also has the unique potential of a recently developed iris-supported lens being put in the eye, maintained in position by passive pupillary miosis, and then dilating the pupil so that the iris will come in front of the lens due to the contour of this lens. The passivity of the miosis precluding synechias, therefore, permits ultimate dilation and positioning of the iris in front of the lens.

What is claimed is:

1. A process for aiding the stabilizing or repositioning of a surgically implanted intraocular lens in the correct position in an eye, characterized by instilling into the eye having the surgically implanted intraocular lens an approximately one drop dose of an ophthalmic solution containing an α-adrenergic blocking agent selected from the group consisting of thymoxamine, phentolamine, azepetine, phenoxybenzamine, clonidine and

totazoline in a concentration of from about 0.1% to about 1% by weight.

2. The process defined by claim 1, characterized by the α-adrenergic blocking agent is thymoxamine.

3. The process defined by claim 1, characterized by the aqueous ophthalmic solution contains thymoxamine in a concentration of about 0.5% by weight.

4. The process defined by claim 1, characterized by the approximately one drop dose is repeated several times per day.

5. The process defined by claim 1, characterized by the approximately one drop dose is instilled daily.

* * * * *